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MINI-REVIEW

International cooperation on health and medical care for viral hepatitis: 30 years of activities on comprehensive viral hepatitis control of the JICA group training program for developing countries

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Abstract: The National Hospital Organization Kumamoto Medical Center has conducted a group training course for health care workers (HCW) from developing countries on viral hepatitis and its related diseases in cooperation with the Japan International Cooperation Agency, for 30 years. In the first 10 years, the course included acquired immunodeficiency syndrome (AIDS), adult T-cell leukemia/lymphoma (ATL), and hepatitis. Following the discovery of the hepatitis C virus and the genotype of the hepatitis B virus, and development of treatments for hepatitis, viral-related cirrhosis, and cancer, the course was divided into two courses. In 2015, the hepatitis training course was renewed as the "Comprehensive Countermeasure for Virus Hepatitis", which ended its role in February 2018. Between 1998 and 2017, 175 HCW from 43 countries, including 36 participants from Egypt, participated. Between October 11 and 20, 2019, we conducted a follow-up survey of the results of the training and conducted a field visit on hepatitis control in Egypt.

***Keywords*:** international cooperation on health and medical care, Japan International Cooperation Agency (JICA), JICA group training program, comprehensive countermeasure of viral hepatitis, developing county

Introduction

Acquired immunodeficiency syndrome (AIDS) and viral hepatitis are serious global issues. There were an estimated 257 million hepatitis B virus (HBV) carriers worldwide in 2015, and HBV-related deaths occurred in an estimated 887,000 patients mostly from cirrhosis and primary liver cancer in 2016 (*1*). Some countries in South-East Asia and Africa have more than 6.2% and 2.0% of their population as carriers, respectively (*1*), and some have more than 20%, presenting a significant health care challenge. Hepatitis A, which is not seen in epidemic numbers in developed countries, is also common in developing countries. The prevention of hepatitis A virus infection is becoming an important issue internationally as international activities, such as the growth in food imports from those countries, increase.

Hepatitis C is a major cause of acute and chronic hepatic diseases, including liver cirrhosis and primary liver cancer. It is estimated that there are as many as 71 million chronically infected people in the world and around 40 thousand people die from hepatitis C virus (HCV)-related diseases (*1*).

Viral hepatitis is an infection that requires urgent development of global measures; thus, collaboration among the international community is essential to implement infection prevention measures and surveillance initiatives to understand the domestic and international situations of hepatitis outbreaks.

The National Hospital Organization Kumamoto Medical Center (NHOKMC) has conducted a group training course for health care workers (HCW) from developing countries in viral hepatitis and its related diseases in cooperation with the Japan International Cooperation Agency (JICA) for 30 years.

Transition of viral hepatitis group training course

In 1988, the NHOKMC made promoting international cooperation on health and medical care one of the basic policies of the hospital. At the request of the JICA, a group training course was started for developing countries by order of the Honorary Director Isao Arita who headed the WHO Smallpox Eradication Unit in 1977-1985 (*2*). The first training course was "Seminar on Blood Transmitted Diseases: Special reference to AIDS, ATL, and Hepatitis", with former Director Fumio Kawano as the course leader. At that time, only HBV was known as a blood transmitted hepatitis virus. In 1989, HCV was discovered (*3*). Investigation of HCV rapidly progressed to not only virology but also

epidemiology and clinical medicine research such as testing, treatments, and clinical course. The seminar on blood transmitted diseases was expanded to include hematology and hepatology; however, it was considered that there was too much content. Hence, in 1998, two courses using material from the AIDS, ATL, and hepatitis courses were created. The first course leader of the hepatitis course was the late Vice President Keishi Kimura (1998-2003).

We planned and formulated training, facilitated lectures and hospital training, accompanied tours at other facilities, and assisted with action plans for hepatitis control after completing the training (2003-2017). For a total of 30 years, the JICA conducted group training activities on hepatitis protection, and supported the dissemination of knowledge on hepatitis in developing countries and the formulation of hepatitis countermeasures. In 2015, the hepatitis course was finally renewed as the "Comprehensive Countermeasure for Virus Hepatitis" course, which ended its role in February 2018.

In the first year of the course in 2003, on the advice of Honorary Director Isao Arita, we avoided duplication of training contents, covered overall viral hepatitis, and enriched the field training with basic and clinical physicians representing Japan as lecturers (Figure 1, Supplemental Figures S1 and S2, *https://www.globalhealthmedicine.com/site/supplementaldata.html?ID=29*). Using the requests and opinions of the trainees at the evaluation meeting at the end of the training, and by learning new diagnostic techniques and treatment methods in the training, we worked to improve our training while reviewing the lecturers and tour facilities. In addition, workshop training was taken from second-type training to active type. We communicated with the trainees, repeated trials and errors, and formulated a training program with high satisfaction. Comparing the data of the evaluation meeting in the first and last years, the program was more highly evaluated in the latter Supplemental Figures S3 and S4 (*https://www.globalhealthmedicine.com/site/supplementaldata.html?ID=29*).

In 2008, Japan worked on comprehensive hepatitis countermeasures, and in December 2009, the Basic Act on Hepatitis Countermeasures was formulated (*4*), which came into effect in January 2010. However, due to the tight national budget, there was a wave of JICA training reductions, and the virus hepatitis course was threatened with closure. In June of the same year, presentation of the necessity of the JICA viral hepatitis course at the Ministry of Foreign Affairs led to its renewal from 2011. However, in 2014, the course was suspended due to the small number of participants, but it was resumed at the request of representatives from Egypt, which had planned to combat hepatitis C as a national project in 2015 until its role ended in February 2018 (Supplemental Figure S5, *https://www.globalhealthmedicine.com/site/supplementaldata.html?ID=29*) (*5*).

Changes in epidemiology, treatment, and countermeasures for viral hepatitis

During this time, the hepatitis C virus was discovered in 1989 (*3*) and hepatitis E in 1990 (*6*). The genotypes

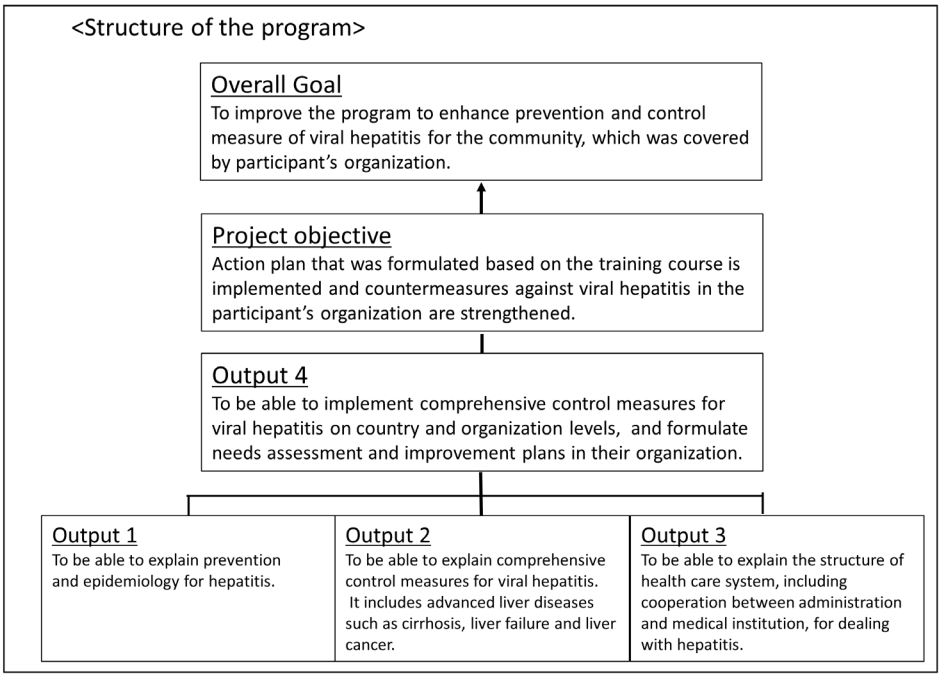

Figure 1. Structure of program. The program consists of six components. Four expected module outputs and project objective, action plan, which was formulated based on the training course is implemented. Overall goal is service for prevention and control measures of viral hepatitis.

of hepatitis B, which have been identified since 1988 (*7*), revealed a difference in clinical features, and the epidemiology of hepatitis has changed significantly (*8*). Furthermore, treatment of viral hepatitis based on these findings, especially advances in interferon (IFN)-based therapy and direct-acting antivirals (DAAs) (*9*) for hepatitis C and nucleic acid analogues (*10*) or pegylated-IFN therapy (*11*) for hepatitis B, were developed. Furthermore, there has been remarkable developments in the management, diagnosis, and treatment of liver cirrhosis and liver cancer caused by viral hepatitis (*12,13*). In 2015, the hepatitis training course was restarted as the "Comprehensive Countermeasure for Viral Hepatitis", which included measures taken by the government in addition to epidemiology, prevention, and treatment.

In 2010, the World Health Organization (WHO) established July 28 as World Hepatitis Day with the aim of preventing the spread of viral hepatitis on a global level, eliminating discrimination and prejudice against patients and infected people, promoting infection prevention, and advocating for the implementation of hepatitis awareness activities, which has increased interest in hepatitis worldwide (*14*). Viral hepatitis is considered the fourth most important infectious disease after the world's three largest infectious diseases (malaria, tuberculosis, and AIDS). More than 500 million people are infected with hepatitis B and C, and hepatitis control is expected to become increasingly important worldwide. In recent years, antiviral treatment has advanced dramatically. Nucleic acid analog treatment for hepatitis B prevents viral reactivation in patients receiving chemotherapy or immunosuppressive drugs, and universal vaccines for infants and children will contribute to a decrease in hepatitis incidence (*15*). Direct-acting antivirals (DAAs) against hepatitis C provide a cure rate of 95% or more within 8-12 weeks treatment. These treatments are being widely carried out in developed and developing countries. The WHO has declared the goal of eliminating viral hepatitis by 2030 (*16*). For this purpose, it is important to treat patients and take comprehensive measures such as infection control that includes resident awareness, picking up infected people, and following up after treatment. This training is in line with that purpose and is expected to help wipe out hepatitis. We have received high evaluations for this course from the trainees who have participated so far.

Between 1998 and 2017, 175 participants from 43 countries participated in this training course. In this period, 36 participants from Egypt participated, 20 of whom participated in the last three years (Supplemental Table S1, *https://www.globalhealthmedicine.com/site/supplementaldata.html?ID=29*) (*17*). Between October 11 and 20, 2019, we conducted a follow-up survey of the results of the training and conducted a field visit on hepatitis control in Egypt (Table 1).

Follow-up survey and hepatitis countermeasure inspection in Egypt

Itinerary

The itinerary on site is Day 1: visit Suez Canal University (Ismailia Province), Day 2: visit two hepatitis centers in Cairo, Day 3: visit Beheira Prefectural Health Department and Hepatitis Center, Day 4: a symposium at the National Institute of Hepatitis and Tropical Medicine (NHTMRI), and Day 5: participation in a three-way meeting between the WHO's Egypt Office, Ministry of Health and Population, and the JICA (Supplemental Figure S6, *https://www.globalhealthmedicine.com/site/supplementaldata.html?ID=29*).

Results and Proposals

The hepatitis C campaign in Egypt was prepared and implemented from October 2018, almost at the same time as the three-year national training in Egypt (October 2015 to February 2018). This country-by-country

Table 1. Anti-HBV response of TCM and related active compounds in clinical trials

Purpose of follow-up

As a follow-up investigation team from JICA Headquarters

- Investigation on the status of hepatitis, especially hepatitis C, in Egypt.
- Confirmation of achievement of action plan by trainees from Egypt.
- Confirmation of our contribution to Egypt so far and its future role.
- Participation in the meeting with WHO Egypt, Ministry of Health and Population (MoHP) and JICA, which participate in consultation on Egypt hepatitis C elimination certification process.
- Visit to Suez Canal University, which participated in the launch of the third country training of JICA and cooperated in the operation.

Results in follow-up survey

The JICA Headquarters confirmed the following as a follow-up investigation team.

- The action plan of the trainees returning from Egypt is being achieved in a short period of time.
- More than 80% of the country's 100 million people have been tested for hepatitis C in Egypt through a national campaign, and treatment has been initiated for those who test positive (testing and treatment costs are free).
- WHO's global elimination of hepatitis C is targeted for 2030, but Egypt could be a global model, with achievement certified in two years.
- In addition to WHO's support, our previous hepatitis control courses have built a foundation for this.
- What can we cooperate with in the future? If the campaign to eliminate hepatitis B in Africa is carried out mainly in Egypt, we may be able to cooperate in the launch and implementation of JICA third country training.

training contributes greatly to the formulation and implementation of hepatitis C measures. Furthermore, the JICA training that has continued for the past 30 years has contributed to these preparation stages. Based on the long history of the JICA hepatitis group training, the NHOKMC is likely to have made a lot of findings, including formulation of measures to find and solve problems for developing countries and the results obtained in Egypt. In addition, the NHOKMC utilized its research to conduct the JICA training, including advice and participation in third-country training, which was scheduled to be mainly deployed in Egypt as well as other African countries. The training included regular surveys of liver cancer after antiviral therapy and liver cancer from non-communicable diseases (*18*), which are a problem after hepatitis C control.

A follow-up study confirmed the following (Table 1): *i*) action plans for trainees returning to Egypt are being achieved in a short period of time; *ii*) hepatitis C in Egypt has been tested by a National Campaign that tested more than 80% of the 100 million people in a year, and treatment was started for positive patients (19); *iii*) the WHO's global hepatitis C sweep is targeted for 2030, but Egypt could be certified as having achieved this in two years and become a global model (20); *iv*) in addition to the WHO's support, our previous hepatitis control courses have built a foundation for future strategies; and *v*) if the campaign to wipe out hepatitis B in Africa is carried out mainly in Egypt, we may be able to cooperate in the launch and implementation of the JICA in a third country. We will continue to build further relationships with Egypt and the JICA.

Conclusion

In the JICA group training course, we comprehensively guided trainees in many developing countries in the epidemiology, prevention, and treatment of viral hepatitis, including liver cirrhosis and liver cancer, as well as administrative measures. Furthermore, we had the opportunity to think about the problems and issues to be overcome in developing countries. This time, as a follow-up survey, we confirmed the activities after training in Egypt. We have confirmed the activities of trainees who were unable to conduct surveys in Egypt, Mongolia, Myanmar, and other countries using social media. In both cases, they utilized their training to achieve the action plan after their return from Japan, and achieved results. Thirty years of international cooperation on health and medical care in the NHOKMC contributed to the practice of comprehensive counter measures for viral hepatitis in developing countries.

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